U.S. Patent Application Ser. No. 05-36,978 Amendment Filed in Response to Office Action Dated 11 April 2003

Amendments to the Claims

Please amend the claims to read as follows:

- 1. (Previously Amended) A method of inducing tumor cell death in a human patient, the method comprising
 - i) locally administering an antigen-releasing agent to a solid tumor in the patient, whereby a tumor antigen is released from cells of the tumor;
 - iia) locally administering to the tumor a leukocyte attractant, whereby leukocytes are induced to infiltrate the tumor; and
 - iib) locally administering to the tumor interferon-gamma (IFN-g) and a second type 1 inflammatory response-(IR1-)promoting agent, whereby a type 1 inflammatory response is induced in the tumor and tumor cell death is induced.
- 2. (Original) The method of claim 1, wherein the antigen-releasing agent is a tumor debulking agent.
- 3. (Original) The method of claim 1, wherein the antigen-releasing agent comprises an agent selected from the group consisting of a proteolytic enzyme, an apoptosis-inducing agent, electrical current, a strong acid, and a strong base.
- 4. (Previously Amended) The method of claim 3, wherein the antigen-releasing agent comprises a proteolytic enzyme selected from the group consisting of trypsin, chymotrypsin, pepsin, and collagenase.
- 5. (Original) The method of claim 3, wherein the antigen-releasing agent comprises only one proteolytic enzyme.
- 6. (Original) The method of claim 3, wherein the antigen-releasing agent comprises at least two proteolytic enzymes.

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- 7. (Original) The method of claim 3, wherein the antigen-releasing agent comprises an alkylphospholipid.
- 8. (Original) The method of claim 7, wherein the alkylphospholipid is an alkylphosphocholine.
- 9. (Previously Amended) The method of claim 7, wherein the alkylphosphocholine is selected from the group consisting of hexadecylphosphocholine and edelfosine.
- 10. (Original) The method of claim 3, wherein the antigen-releasing agent is electrical current delivered by way of electrodes inserted into the tumor.
- 11. (Currently Amended) The method of claim 3, wherein the antigen-releasing agent comprises a strong acid selected from the group consisting of eoncentrated hydrochloric acid and eoncentrated sulfuric acid.
- 12. (Currently Amended) The method of claim 3, wherein the antigen-releasing agent comprises a strong base selected from the group consisting of eoncentrated sodium hydroxide and eoncentrated potassium hydroxide.
- 13. (Original) The method of claim 1, wherein the antigen-releasing agent is administered to the tumor at least two hours before administering the leukocyte attractant to the tumor.
- 14. (Original) The method of claim 1, wherein the antigen-releasing agent and the leukocyte attractant are co-administered to the tumor.
- 15. (Original) The method of claim 1, wherein the antigen-releasing agent is administered to the tumor at least two hours before administering IFN-g to the tumor.

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- 16. (Original) The method of claim 1, wherein the antigen-releasing agent and the IFN-g are co-administered to the tumor.
- 17. (Original) The method of claim 1, wherein the leukocyte attractant comprises a monocyte attractant.
- 18. (Original) The method of claim 17, wherein the monocyte attractant is selected from the group consisting of MCP-1, MCP-2, MCP-3, and MCP-4.
- 19. (Original) The method of claim 1, wherein the leukocyte attractant comprises a T cell attractant.
- 20. (Original) The method of claim 19, wherein the T cell attractant is selected from the group consisting of RANTES, IP-10, and Mig.
- 21. (Original) The method of claim 1, wherein the leukocyte attractant comprises a granulocyte attractant.
- 22. (Original) The method of claim 21, wherein the granulocyte attractant is selected from the group consisting of interleukin-8, granular component P-2, growth-related oncogen-1, growth-related oncogen-2, growth-related oncogen-3, neutrophil activated protein, and neurotactin.
- 23. (Original) The method of claim 21, wherein the granulocyte attractant is a eosinophil attractant.
- 24. (Original) The method of claim 23, wherein the eosinophil attractant is eotaxin.

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25. (Original) The method of claim 1, wherein the leukocyte attractant is coadministered with at least one of IFN-g and the second IR1-promoting agent.

- 26. (Original) The method of claim 1, wherein the leukocyte attractant and at least one of IFN-g and the second IR1-promoting agent are administered not more than two hours apart.
- 27. (Original) The method of claim 1, wherein the leukocyte attractant and at least one of IFN-g and the second IR1-promoting agent are administered more than two hours apart.
- 28. (Original) The method of claim 1, wherein the leukocyte attractant and at least one of IFN-g and the second IR1-promoting agent are co-administered.
- 29. (Previously Amended) The method of claim 1, wherein the second IR1-promoting agent is selected from the group consisting of interleukin-2 (IL-2), interleukin-12 (IL-12), tumor necrosis factor-alpha (TNF-a), and tumor necrosis factor-beta (TNF-b).
- 30. (Original) The method of claim 29, wherein the second IR1-promoting agent comprises IL-2.
- 31. (Original) The method of claim 29, wherein the second IR1-promoting agent comprises TNF-b.
- 32. (Original) The method of claim 29, wherein the second IR1-promoting agent comprises both IL-2 and TNF-b.
- 33. (Original) The method of claim 1, wherein multiple aliquots of each of IFN-g and the second IR1-promoting agent are administered to the patient, and wherein at least 48 hours elapse between aliquots.

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- 34. (Original) The method of claim 1, wherein IFN-g and the second IR1-promoting agent are co-administered.
- 35. (Original) The method of claim 1, wherein IFN-g and the second IR1-promoting agent are separately administered not more than two hours apart.
- 36. (Original) The method of claim 1, wherein IFN-g and the second IR1-promoting agent are separately administered more than two hours apart.
- 37. (Original) The method of claim 1, further comprising
 - iii) locally administering to the tumor a type 1 lymphocyte attractant in order to sustain the type 1 inflammatory response.
- 38. (Original) The method of claim 37, wherein the type 1 lymphocyte attractant is selected from the group consisting of RANTES, IP-10, and Mig.
- 39. (Original) The method of claim 37, wherein the type 1 lymphocyte attractant comprises IP-10 and Mig.
- 40. (Original) The method of claim 37, further comprising

 iv) sustaining the type 1 inflammatory response by locally administering autologous leukocytes to the tumor.
- 41. (Original) The method of claim 37, further comprising
 - iv) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced.

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- 42. (Original) The method of claim 41, further comprising
 - v) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.
- 43. (Original) The method of claim 37, further comprising
 - iv) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.
- 44. (Original) The method of claim 1, further comprising
 - iii) locally administering autologous leukocytes to the tumor.
- 45. (Original) The method of claim 44, wherein the autologous leukocytes are obtained from the patient and expanded prior to locally administering them to the tumor.
- 46. (Previously Amended) The method of claim 44, wherein the autologous leukocytes are obtained from the patient and contacted with an independently-selected IR1-promoting agent prior to locally administering them to the tumor.
- 47. (Previously Amended) The method of claim 44, wherein the autologous leukocytes are obtained from the patient, expanded ex vivo, and contacted with an independently-selected IR1-promoting agent prior to locally administering them to the tumor.
- 48. (Previously Amended) The method of claim 47, wherein the leukocytes are contacted with both the independently-selected IR1-promoting agent and with at least one of interferon-alpha (IFN-a) and IL-12 prior to locally administering them to the tumor.
- 49. (Original) The method of claim 44, further comprising
 - iv) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced.

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- 50. (Original) The method of claim 49, further comprising
 - v) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.
- 51. (Original) The method of claim 44, further comprising
 - iv) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.
- 52. (Original) The method of claim 1, further comprising
 - iii) administering a memory cell-inducing agent to the patient after inducing the type 1 inflammatory response, whereby production of anti-tumor type 1 immune memory cells is enhanced.
- 53. (Original) The method of claim 52, wherein the memory cell-inducing agent is selected from the group consisting of interleukin-15 (IL-15) and IFN-a.
- 54. (Original) The method of claim 52, wherein the memory cell-inducing agent is IL-15.
- 55. (Original) The method of claim 52, wherein the memory cell-inducing agent is IFN-a.
- 56. (Original) The method of claim 52, wherein the memory cell-inducing agent is administered after the tumor shrinks to less than 10 percent of its size immediately prior to administration of the antigen-releasing agent.
- 57. (Original) The method of claim 1, further comprising supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral.

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- 58. (Original) The method of claim 57, wherein the vitamin is selected from the group consisting of vitamins A, B, C, D, and E.
- 59. (Original) The method of claim 58, wherein the vitamin is vitamin C and wherein the patient's nutrition is supplemented such that the patient receives from 200 to 400 milligrams of vitamin C daily.
- 60. (Original) The method of claim 58, wherein the vitamin is vitamin E and wherein the patient's nutrition is supplemented such that the patient receives from 200 to 400 international units of vitamin E daily.
- 61. (Original) The method of claim 57, wherein the mineral is selected from the group consisting of selenium, zinc, calcium, magnesium, iron, and copper.
- 62. (Original) The method of claim 61, wherein the mineral is selenium and wherein the patient's nutrition is supplemented such that the patient receives from 200 to 400 micrograms of selenium daily.
- 63. (Original) The method of claim 61, wherein the mineral is zinc and wherein the patient's nutrition is supplemented such that the patient receives from 15 to 100 milligrams of zinc daily.
- 64. (Original) The method of claim 57, wherein the patient's nutrition is supplemented beginning at least on the same day that the antigen-releasing agent is administered to the tumor, and continuing through at least the same day that IFN-g is administered to the tumor.
- 65. (Original) The method of claim 57, wherein the patient's nutrition is supplemented beginning at least five days before the antigen-releasing agent is administered to the

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tumor, and continuing through at least three days after the day that IFN-g is administered to the tumor.

- 66. (Previously Amended) A method of inducing tumor cell death in a human patient, the method comprising
 - i) supplementing the patient's nutrition with a nutrient selected from the group consisting of a vitamin and a mineral;
 - ii) locally administering an antigen-releasing agent to a solid tumor in the patient, whereby a tumor antigen is released from cells of the tumor;

thereafter

- iiia) locally administering to the tumor a leukocyte attractant, whereby leukocytes are induced to infiltrate the tumor; and
- iiib) locally administering to the tumor interferon-gamma (IFN-g) and a second type 1 inflammatory response-(IR1-)promoting agent, whereby a type 1 inflammatory response is induced in the tumor;

thereafter

- iv) sustaining the type 1 inflammatory response by
 - iva) locally administering to the tumor a type 1 lymphocyte attractant,
 - ivb) locally administering autologous leukocytes to the tumor, or
 - ivc) both iva) and ivb);

and thereafter

v) administering a memory cell-inducing agent to the patient after inducing the
 type 1 inflammatory response, whereby production of anti-tumor type 1
 immune memory cells is enhanced and tumor cell death is induced.

67-80. (Canceled)

- 81. (New) A method of inducing a type 1 inflammatory response at the site of a solid tumor in a human patient, the method comprising
 - i) locally administering an antigen-releasing agent to the tumor;

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- iia) locally administering to the tumor a leukocyte attractant; and
- iib) locally administering to the tumor interferon-gamma (IFN-g) and a second type 1 inflammatory response-(IR1-)promoting agent.
- 82. (New) A method of inducing tumor cell death in a human patient, the method comprising
 - i) locally administering an antigen-releasing agent to a solid tumor in the patient, whereby a tumor antigen is released from cells of the tumor;
 - iia) locally administering to the tumor a leukocyte attractant, whereby leukocytes are induced to infiltrate the tumor; and
 - iib) locally administering to the tumor interferon-gamma (IFN-g) and a second type 1 inflammatory response-(IR1-)promoting agent, in an amount effective to induce a type 1 inflammatory response in the tumor, whereby tumor cell death is induced.
- 83. (New) A method of inducing tumor cell death in a human patient, the method comprising locally co-administering to a solid tumor in the patient:
 - i) an antigen-releasing agent;
 - ii) a leukocyte attractant;
 - iii) interferon-gamma (IFN-g); and
 - iv) a second type 1 inflammatory response-(IR1-) promoting agent.